Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 117 to 220 are pending in the application, with 117, 127, 135, 143, 151, 160, 176, 184, 191, and 210 being the independent claims. Claims 23 to 116 are sought to be cancelled without prejudice to or disclaimer of the subject matter therein. New claims 117 to 220 are sought to be added. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

I. Information disclosure statement.

The examiner notes that the U.S.P.T.O was unable to find the references submitted with the information disclosure statement and form 1449, filed October 2, 2001. As a courtesy, Applicants enclose copies of the aforementioned references in addition to copies of the Information Disclosure Statement and form 1449, originally filed October 2, 2001.

II. Objection to the Specification

As requested by the Examiner, the specification has been amended to account for the issuance of Application 09/006,353 as United States Patent No. 6,261,801.

III. Rejections under 35 U.S.C. § 112, first paragraph, written description

The Examiner has rejected claims 23-25, 27, 28, 30, 31, 33-44, 46-54, 57, 58, 61, 62, 65-71, 73-87, 101-102, 104, 105, 107, 108 and 110-116 under 35 U.S.C. § 112, first paragraph, as allegedly "containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." *See*, Paper No. 8, page 4.

Applicants respectfully traverse. Applicants assert that each of the claims pending prior to and after the present amendment is fully supported and satisfies the statutory written description requirements under 35 U.S.C. § 112.

Presently rejected claims 23-25, 27, 28, 30, 31, 33-44, 46-54, 57, 58, 61, 62, 65-71, 73-87, 101-102, 104, 105, 107, 108 and 110-116 have been canceled without prejudice or disclaimer. While not wishing to acquiesce to the Examiner's assertion, and solely to advance prosecution, Applicants have added new claims 126 to 150 and 160 to 220, which recite a functional element. The present rejection will be addressed in so far as it is understood by Applicants to apply to claims newly added herein.

In an analysis of written description under 35 U.S.C. § 112, first paragraph, the Examiner bears the initial burden of presenting a *prima facie* case of unpatentability. This burden is only discharged if the Examiner can present evidence or reasons why one skilled in the art would not reasonably conclude that Applicants possessed the subject matter as of the priority date of the present application. *In re Wertheim*, 541 F.2d 257, 262, 191

U.S.P.Q.2d 90, 96 (C.C.P.A. 1976); M.P.E.P. § 2163.04. In the instant case, Applicants maintain that the Examiner has not met this burden.

The test for the written description requirement is whether one skilled in the art could reasonably conclude that the inventor had possession of the claimed invention based on the specification as filed. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 U.S.P.Q.2d 1111, 1116 (Fed. Cir. 1991); M.P.E.P. § 2163.02. Indeed, as the Federal Circuit has noted, "the issue is whether one of skill in the art could derive the claimed ranges from the patent's disclosure." *Union Oil Company of California v. Atlantic Richfield Company*, 208 F.3d 989, 54 U.S.P.Q. 2d 1227 (Fed. Cir. 2000) (emphasis added).

Pending claims stand rejected because they encompass polypeptides which are alleged not to be functionally or structurally limited beyond the disclosed amino acid sequence. More specifically, the Examiner alleges that "[t]he instant specification discloses, however, a single isolated polypeptide sequence SEQ ID NO:2. Given the unpredictability of altering amino acids in proteins and retaining activity, and the fact that the specification fails to provide objective evidence that the additional sequences are indeed species of the claimed genus it cannot be established that a representative number of species have been disclosed to support the genus claim." *See*, Paper No. 8, page 5.

However, it is well established that a "gene is a chemical compound, albeit a complex one". *Amgen, Inc. v. Chugai Pharamceutical Co., LTD.*, 927 F.2d 1200, 1206 (Fed. Cir. 1991). Thus, the claims of the instant application, directed to particular polypeptides of the disclosed amino acid sequence of SEQ ID NO:2, as encoded by the nucleic acid sequence of SEQ ID NO:1, are essentially chemical claims involving generic chemical formulae. As stated by Judge Lourie in *University of California v. Eli Lilly*, 119

F.3d 1559 (Fed. Cir. 1997), "In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass." All of the objectives met by a generic chemical formula are similarly met by the explicit description in the instant specification of a polynucleotide sequence (*i.e.* SEQ ID NO:1) and the amino acid sequence encoded thereby (SEQ ID NO:2) and by the instant claims to polypeptides consisting of the full-length, full-length minus N-terminal methionine, and mature polypeptides having the amino acid sequence of SEQ ID NO:2; the full-length, full-length minus N-terminal methionine, and mature polypeptides having the amino acid sequence encoded by the cDNA contained in ATCC Deposit No. 97788; polypeptides consisting of at least 30 or 50 amino acids of SEQ ID NO:2; and polypeptides having a recited percent identity to SEQ ID NO:2. That is, the instant claims clearly distinguish the boundaries of the claimed genera and identify all of the members of those genera. Accordingly, one skilled in the art would reasonably conclude that Applicants had possession of the polypeptides encompassed by the rejected claims upon reading the present application as filed, and would immediately recognize that the Applicants had "invented what is claimed" (*Vas-Cath*, 935 F.2d at 1563). Therefore, the specification contains an adequate written description of the claimed polypeptides. Applicants have provided the skilled artisan with a "generic formula" in the form of the amino acid sequence of SEQ ID NO:2, which indicates "with specificity what the generic claims encompass." Armed with this information "one skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass."

Furthermore, the specification particularly teaches on embodiments of the invention rejected by the Examiner in the present action. Polypeptides consisting of at least 30 and/or at least 50 amino acid residues of SEQ ID NO:2 are taught, for example, at page 31, line 27 through page 32, line 4; polypeptides having at least 90% or 95% identity to SEQ ID NO:2 are taught, for example, at Page 31, line 27 through Page 32, line 32; and polypeptides which specifically bind antibodies specific for a polypeptide having the amino acid sequence of SEQ ID NO:2 are taught, for example, at Page 33, lines 7-16.

For example, the skilled artisan could clearly envision each of the polypeptides comprising at least 30 contiguous amino acids, of SEQ ID NO:2 as a progression, *i.e.*, polypeptides comprising amino acids 1-30, 2-31, 3-32, etc. The skilled artisan could certainly further envision sequentially adding contiguous amino acids to either end of any of the described embodiments. Indeed, nothing more than what is described in the specification would be required for the skilled artisan to identify every single one of the polypeptides and polypeptide fragments containing at least 30 (or at least 50) amino acids of SEQ ID NO:2. Likewise, the skilled artisan could easily substitute any given amino acid for any other given amino acid, or add or delete amino acids, such that nothing more than what is described in the specification would be required to identify every single one of the polypeptides comprising amino acid sequences that are at least 90% (or at least 95%) identical to the amino acid sequence of SEQ ID NO:2. Thus, it would be readily apparent to the skilled artisan that the Applicants had "invented what is claimed" (*Vas-Cath*, 935 F.2d at 1563).

Accordingly, one skilled in the art, enlightened by the teachings of the present application, could readily envision all of the various polynucleotide sequences that comprise the specified polynucleotides.

Applicants respectfully assert that the specification conveys with reasonable clarity that Applicants were in possession of the claimed invention. The entire claimed genus of polypeptides is described such that a skilled artisan would recognize that Applicants were in possession of the genus. Further, because the claims recite amino acid molecules which consist of portions of the amino acid sequence of SEQ ID NO:2, and the claimed variant polypeptides bind an antibody with specificity for a reference polypeptide consisting of amino acids 1-233 of SEQ ID NO:2, the claims do not read on undescribed amino acid sequences.

Furthermore, Applicants assert that the claims are adequately described under the PTO's written description guidelines. According to the guidelines:

> [t]he written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by . . . disclosure of relevant, identifying characteristics, *i.e.*, [1] structure or other physical and/or chemical properties, [2] by functional characteristics . . . ***or*** [3] by a combination of such identifying characteristics.

Guidelines for Examination of Patent Applications Under the 35 U.S.C. § 112, ¶1, *"Written Description" Requirement*, 66 Fed. Reg. 1104, 1106 (Jan. 5, 2001) ("*Written Description Guidelines*") (emphasis added).

Thus, the guidelines indicate that a representative species may be adequately described through its structure, through its functional characteristics, ***or*** through a

combination of its structure and function.

Applicants assert that the polypeptides embodied in the new claims are described by both a structure (related to an amino acid sequence) and a functional characteristic (binding to an antibody). Recitation of the primary structure of the polypeptide and the functional test defines a genus and indicates possession of the genus.

Applicants assert that the new claims fully meet the written description requirements of 35 U.S.C. § 112, first paragraph under the test set out in the PTO's *Written Description Guidelines*. Moreover, Applicants assert that the specification conveys with reasonable clarity that Applicants were in possession of the claimed invention and that the claims are fully supported by the specification. Finally, Applicants respectfully assert that the Examiner has failed to meet the required burden in presenting evidence or reasons why those skilled in the art would not recognize the claimed invention from the disclosure. For all of the above reasons, Applicants assert that the written description requirements have been met and that the Examiner's rejection is overcome. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph, is respectfully requested.

IV. Rejections under 35 U.S.C. § 112, First Paragraph, Enablement

The Examiner has rejected claims 39 to 51 and 101 to 116 under 35 U.S.C. § 112, first paragraph, as allegedly containing "subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention." *See*, Paper No. 8, page 6.

Presently rejected claims 39 to 51 and 101 to 116 have been canceled without prejudice or disclaimer. Accordingly, the present rejection will be addressed in so far as it is understood by Applicants to apply to pending claims newly added herein.

Applicants respectfully direct the Examiner's attention to the attached Statement Concerning the Deposited cDNA Clone, executed by an attorney of record, Kenley K. Hoover, on December 16, 2002. The Statement assures that the TNFR5 cDNA has been deposited at an acceptable depositary and that the criteria set forth in 37 C.F.R. §§ 1.801-1.809 have been met. Accordingly, Applicants respectfully request that the instant rejection of the claims directed to the cDNA clone contained in ATCC Deposit No. 97788, on grounds of inaccessibility of the claimed cDNA, should be reconsidered and withdrawn.

V. Rejections under 35 U.S.C. § 112, second paragraph, indefiniteness

The Examiner rejected claims 73 and 75 under 35 U.S.C. § 112, second paragraph, as allegedly "being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." *See*, Paper No. 8, page 6. Applicants respectfully traverse.

More specifically, the Examiner alleges that claim 73 is indefinite as it encompasses a polypeptide comprising amino acids 215-233 of SEQ ID NO:2 while being dependent from claim 71, which encompasses a polypeptide comprising 30 contiguous amino acids from amino acids 1-233 of SEQ ID NO:2. The Examiner further alleges that claim 75 is indefinite as it encompasses a polypeptide which binds an antibody specific for a polypeptide comprising amino acids –26 to 233 of SEQ ID NO:2 while being dependent

from claim 71, which encompasses a polypeptide comprising 30 contiguous amino acids from amino acids 1-233 of SEQ ID NO:2. See, Paper No. 8, pages 6-7.

Applicants respectfully point out that rejected claim 73 incorporates all the limitations of claim 71 from which it depends, and further limits the claimed polypeptides in so much as they further comprise 215-233 of SEQ ID NO:2. Furthermore, rejected claim 75 incorporates all the limitations of claim 71 from which it depends, and further functionally limits the claimed polypeptides in so much as they further bind an antibody specific for a polypeptide comprising amino acids –26-233 of SEQ ID NO:2. Accordingly, Applicants assert that each of the rejected claims pending prior to the present amendment is fully supported and satisfies the statutory definiteness requirements under 35 U.S.C. § 112.

However, Applicants note that presently rejected claims 73 and 75 have been canceled without prejudice or disclaimer. Accordingly, the present rejection has been obviated and Applicants respectfully request that it be reconsidered and withdrawn.

VI. Rejections under 35 U.S.C. § 103

The Examiner has rejected claims 71 and 74 to 87 under 35 U.S.C. § 103(a) as allegedly "being unpatentable over Hillier *et al.*, Database EST, Genbank Accession No. AA150541, May 19, 1997 (cited by Applicants), in view of Sibson et al. WO 94/01548 and Mosley et al. US Patent No. 5,783,672, filing date Sept. 12, 1994." *See*, Paper No. 8, pages 7-8. The Examiner alleges that the present application is not entitled to benefit under 35 U.S.C. § 120 of Provisional Application Serial No. 60/035,496, filed January 14, 1997, and

therefore awards the present application a priority date of August 7, 1997. Applicants respectfully disagree and traverse this rejection.

Applicants respectfully point out that benefit under 35 U.S.C. § 120 is not sought, but that benefit of the earlier filed provisional application under 35 U.S.C. § 119(e) has been requested in the instant case. Applicants contend that each of the claims allegedly unpatentable over Hillier *et al.*, in view of Sibson et al. and Mosley et al., is fully supported and satisfies the statutory requirements of 35 U.S.C. § 101. Furthermore, Applicants contend that such support is also found in Provisional Application No. 60/035,496, as originally filed, and that this provisional application is therefore properly available under 35 U.S.C. § 119(e). Accordingly, Applicants contend that January 14, 1997 is the correct priority date of the present application.

Furthermore, the Examiner has not set forth reasons why Provisional Application No. 60/035,496, as originally filed, does not satisfy current utility guidelines.

> Any rejection based on lack of utility should include a detailed explanation why the claimed invention has no specific and substantial credible utility. Whenever possible, the examiner should provide documentary evidence ... to support the factual basis for the *prima facie* showing. ... If documentary evidence is not available, the examiner should specifically explain the scientific basis for his or her factual conclusions.

See, M.P.E.P. § 2107(II)(C) at [2100-30] (August 2001). The Examiner has not put forward any explanation stating why the current utility guidelines have not been met and therefore has not met the required burden. Hence, Applicants respectfully contend that the present rejection in improperly based and request its reconsideration and withdrawal.

However, Applicants note that the effective date for Hillier *et al.* was December 10, 1996, not May 19, 1997 as asserted by the Examiner. Nonetheless, Applicants assert that Hillier *et al.* cannot and should not be cited against Applicants.

Applicants respectfully point out that "[t]o establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations." *See*, M.P.E.P. § 2142 at [2100-121]. Care must be exercised not to use the Applicants' disclosure to fill in the gaps in the prior art. *In re Vaeck*, 947 F.2d 488, 493, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991); *In re Grabiak*, 769 F.2d 729, 226 U.S.P.Q. 870 (Fed. Cir. 1985). Further, the Federal Circuit has stated time and again that it is impermissible within the framework of a Section 103 rejection to pick and choose from any one reference only so much of it as will support a given position to the exclusion of other parts necessary for the full appreciation of what the reference fairly suggests to one of ordinary skill in the art. One cannot consider a reference in less than the entirety, *i.e.*, disregard disclosures in the reference that diverge from and teach away from the invention. *In re Hedges*, 783 F.2d 1038, 1041, 228 U.S.P.Q. 685, 687 (Fed. Cir. 1986).

Applicants contend that the references cited by the Examiner do not teach or suggest all of the elements of the instant claims. Further, there is no suggestion to combine the reference teachings. Thus, the Examiner has not established a *prima facie* case of obviousness under 35 USC § 103(a).

The Examiner has determined that "Hillier et al. discloses a cDNA clone that is 100% identical to nucleotides 594-777 of the nucleic acid sequence of SEQ ID NO:1, and which encodes amino acids 112-172 of the protein of SEQ ID NO:2 (61 amino acids)." *See*, Paper No. 8, page 8. Applicants respectfully disagree. The Hillier reference discloses a nucleic acid sequence that shares 95% identity with nucleotides 346 to 777 of SEQ ID NO:1 of the present invention. *See*, Paper No. 8, Examiner's sequence alignment. Applicants note that Hillier discloses this nucleotide sequence in a research publication entitled "Generation and analysis of 280,000 human expressed sequence tags," which was published in the journal Genome Research. *See*, Paper No. 8, Examiner's sequence alignment. Applicants further note that Hillier identifies the nucleotide sequence it but does not teach the identity or importance of any polypeptide it may encode. *See*, Paper No. 8, Examiner's sequence alignment. Furthermore, Hillier does not disclose the identity of any start or stop codon, it does not indicate a correct reading frame, or even a correct sense or orientation.

Applicants respectfully contend that there is no suggestion or motivation to combine the references relied upon by the Examiner in the present rejection. Hillier does not provide any motivation to select the sequence relied on by the Examiner from the "280,000 human expressed sequence tags" they claim to have identified. Nor does Hillier provide any suggestion or motivation to select that portion of this sequence which shares 100% identity with SEQ ID NO:1 of the present application. Thus, one of ordinary skill in the art who was in possession of the teachings of Hillier *et al.* would not have been motivated to combine the sequence of Genbank Accession No. AA150541 with any other reference to arrive at any

polypeptide embodiment of the instant claims.

Further, the other two cited references do not cure the deficiencies of Hillier *et al.* As the Examiner has noted, Sibson *et al.* discloses how to express cDNA from an expression vector and eukaryotic host, while Mosley *et al.* discloses compositions comprising a polypeptide and a carrier, as well as fusion proteins. *See*, Paper No. 8, pages 8-9. However, it is implicit in Sibson *et al.* and Mosley *et al.* that one need be in possession of a nucleotide sequence known to encode a protein, or an actual amino acid sequence, in order to benefit from their teachings and directions. One of ordinary skill in the art, upon reading Sibson *et al.* and/or Mosley *et al.* would have no motivation to combine these references with any sequence of Hillier et al., or more specifically to combine with the sequence of Ganbank Accession No. AA150541 to achieve any polypeptide embodiment of the claimed invention.

Therefore, it is improper to use Hillier *et al.*, either alone or in combination with any other reference, as a prior art reference in rejecting the polypeptides of the claimed invention under 35 U.S.C. § 103(a).

Applicants further note that newly added claims 176 to 183 also possess a functional element: that the polypeptide bind an antibody with specificity for a reference polypeptide consisting of amino acids 1 to 233 of SEQ ID NO:2. This functional element is neither taught nor suggested by the cited references. Hence, Applicants assert that references are

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicant(s) therefore respectfully request(s) that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicant(s) believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Elizabeth J. Haanes, Ph.D.
Registration No. 42,613

Date: December 27, 2002

1100 New York Avenue, N.W.
Suite 600
Washington, D.C. 20005-3934
(202) 371-2600

Version with markings to show changes made

Claims 23 to 116 are sought to be cancelled.

New claims 117-212 are sought to be added.

The pending first paragraph on page 1 is sought to be replaced with the following paragraph:

This application is a divisional of U.S. Patent Application No. 09/006,353, filed January 13, 1998, now United States Patent No. 6,261,801, which claims benefit of U.S. Provisional Application Serial Nos. 60/035,496, filed January 14, 1997, and 60/054,885, filed August 7, 1997. Each of these applications are incorporated herein by reference in [its] their entireties.